UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,358	10/16/2001	Rembert Pieper	42521	3368

22878 7590 09/12/2006

AGILENT TECHNOLOGIES INC.
INTELLECTUAL PROPERTY ADMINISTRATION, M/S DU404
P.O. BOX 7599
LOVELAND, CO 80537-0599

EXAMINER	
VENCI, DAVID J	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 09/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,358	PIEPER ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 7, 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,52,62-69,84,85,88,89,104-107 and 110-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,52,62-69,84,85,88,89,104-107 and 110-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges Applicants' reply, filed August 7, 2006, which amends claims 63 and 104, and adds new claims 110-113.

Currently, claims 32, 52, 62-69, 84-85, 88-89, 104-107 and 110-113 are under examination

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Specifically, the specification does not appear to provide antecedent basis for the language "specific predefined proteins" as recited in claims 63 and 84. Correction is required.

Claim Rejections - 35 USC § 112

Claims 32, 52, 62-69, 84-85, 88-89, 104-107 and 110-113 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 63 and 84, the recitation of "specific predefined proteins" is indefinite and lacks antecedent support in the specification. The identity of objects and/or steps required for "predefining" proteins is not clear.

In claim 63, the recitation of "each solid phase matrix comprises a plurality of particles" is indefinite, wherein "each solid phase matrix" = a bead (see specification p. 9, lines 10-11, "[a] suitable matrix is, for example a bead or a microbead shape") (emphases added). Whether/how a bead comprises "a plurality of particles" is not clear.[1]

In claim 84, the recitation of "each solid phase matrix comprises a plurality of particles" is indefinite, wherein "each solid phase matrix" = a bead (see specification p. 9, lines 10-11, "[a] suitable matrix is, for example a bead or a microbead shape") (emphases added). Whether/how a bead comprises "a plurality of particles" is not clear.[2]

In claim 63, the recitation of "a first and second solid phase matrix contacting each other" is indefinite, wherein "each solid phase matrix" = beads (see specification p. 13, lines 4-7, "the matrix is loose beads... matrix beads") (emphases added). Whether/how a matrix of beads is in contact with another matrix of

---

[1] Applicants may obviate this rejection by amending the affected phrase as follows: a first and a second solid phase matrix contacting each other, wherein each solid phase matrix comprises a ~~plurality of particles~~ particle, and wherein the particles of the first and second solid phase matrices are present as a mixture in said affinity binding composition;

[2] Applicants may obviate this rejection by amending the affected phrase as follows: a plurality of solid phase matrices arranged such that each solid phase matrix is in contact with at least one other solid phase matrix; and... wherein each solid phase matrix comprises a ~~plurality of particles~~ particle, and wherein the particles are present in the affinity binding composition as a mixture;

beads is not clear. Whether the claim limitation "contacting" requires a matrix of beads to be stacked, layered and/or adjoined on/to another matrix of beads is not clear. How a matrix of beads that is stacked, layered and/or adjoined on/to another matrix of beads can be "present as a mixture" is not clear.[3]

In claim 84, the recitation of "each solid phase matrix is in contact with at least one other solid phase matrix" is indefinite, wherein "each solid phase matrix" = beads (see specification p. 13, lines 4-7, "the matrix is loose beads... matrix beads") (emphases added). Whether/how a matrix of beads is in contact with another matrix of beads is not clear. Whether the claim limitation "in contact" requires a matrix of beads to be stacked, layered and/or adjoined on/to another matrix of beads is not clear. How a matrix of beads that is stacked, layered and/or adjoined on/to another matrix of beads can be present "as a mixture" is not clear.[4]

[3] Applicants may obviate this rejection by amending the affected phrase as follows: a first and a second solid phase matrix contacting each other, wherein each solid phase matrix comprises a plurality of particles~~, and wherein the particles of the first and second solid phase matrices are present as a mixture in said affinity binding composition~~;

[4] Applicants may obviate this rejection by amending the affected phrase as follows: a plurality of solid phase matrices arranged such that each solid phase matrix is in contact with at least one other solid phase matrix; and... wherein each solid phase matrix comprises a plurality of particles~~, and wherein the particles are present in the affinity binding composition as a mixture~~;

Claim Rejections - 35 USC § 102

Claims 32, 52, 62-69, 89, 104, 110 and 112 are rejected under 35 U.S.C. 102(b) as being anticipated by Stausbøl-Grøn *et al.*, 391 FEBS LETTERS 71 (1996).

Stausbøl-Grøn *et al.* describe a method for separating proteins (see p. 71, right column, last paragraph, second sentence, "single-chain Fv antibody fragments (scFv)"; *see also* Section 1 *Introduction*, first sentence, "coat protein") from a sample (see Section 2.4 *Competitive two solid phase biopanning-protein mixture*, second paragraph, "[a]n aliquot of 10^{12} colony-forming units (cfu) from the naïve library, and competitive soluble MIX protein"; *see also* Section 2.5 *Competitive two solid phase biopanning-cytosolic cell extract from a melanoma cell line*, fourth sentence, "naïve library (10^{12} cfu) and competitive soluble FM55p proteins") that contains proteins and recovering a modified sample (see Abstract, "enrich selectively phage displayed antibodies directed against proteins constituting a difference between two populations of cells") comprising the steps of:

(1) removing (see p. 72, col. 1, fifth paragraph, "immunobead was washed") at least two specific predefined proteins (see p. 73, col. 2, second paragraph, "Competitive proteins", see Fig. 2(A), MIX+LDH versus MIX; *see also* Section 3 *Results and discussion*, p. 74, right column, second full paragraph, first sentence, "selection inhibition of all similarities"; *see also* last sentence, "as many proteins as possible") (emphasizing plurality of proteins) from a sample that contains the at least two specific predefined proteins, thereby

(2) producing and/or recovering the modified sample containing a plurality of proteins that was present in the sample (see Abstract, "enrich selectively phage displayed antibodies directed against proteins constituting a difference between two populations of cells") prior to removal of the at least two specific predefined proteins;

wherein the removing step comprises contacting the sample with an affinity binding composition (see Fig. 1, "two solid phase system") comprising:

(a) a first and second solid phase matrix (see Fig. 1, "two solid phase system") contacting each other (see Fig. 1, "immunobeads in an immunotube"), wherein each solid phase matrix comprises a plurality of particles (see Fig. 1, "immunobeads in an immunotube"), wherein the particles are present in a mixture (see p. 72, col. 1, sixth paragraph, "4 ml 2% MPBS... five immunobeads... were added");

(b) a first receptor (see Fig. 1, "LDH") immobilized on said first solid phase matrix (see Fig. 1, "immunobeads); and

(c) a second receptor (see Fig. 1, "MIX proteins") immobilized on said second solid phase matrix (see Fig. 1, "immunotube").

With respect to claims 64-69, Stausbøl-Grøn *et al.* describe a method wherein "different coating conditions in parallel" is performed "to cover as many proteins as possible" (see p. 74, col. 2, second full paragraph, last sentence).

Claims 32, 52, 62, 84, 89, 104, 111 and 113 are rejected under 35 U.S.C. 102(b) as being anticipated by Stausbøl-Grøn *et al.*, 391 FEBS LETTERS 71 (1996).

Stausbøl-Grøn *et al.* describe a method for separating (see Abstract, first sentence "enrich selectively"; *see also* Abstract, second sentence, "isolated"; *see also* Fig. 1, bottom, "rescued"; *see also* Section 3 *Results and discussion*, p. 73, right column, first paragraph, second sentence, "obtain"; *see also* Section 3 *Results and discussion*, p. 73, right column, third paragraph, first sentence, "enrich preferentially"; *see also* Section 3 *Results and discussion*, p. 74, right column, second full paragraph, first sentence, "selection") proteins (see p. 71, right column, last paragraph, second sentence, "single-chain Fv antibody fragments (scFv)"; *see also* Section 1 *Introduction*, first sentence, "coat protein") from a sample (see p. 71, right column, last paragraph, second sentence, "naïve phagemid library") that contains proteins and recovering a modified sample comprising the steps of:

(1) removing at least two specific predefined proteins (see Section 3 *Results and discussion*, p. 74, right column, second full paragraph, first sentence, "selection inhibition of all similarities"; *see also* last sentence, "as many proteins as possible") (emphasizing plurality of proteins) from a sample, thereby

(2) producing and/or recovering the modified sample (see Abstract, first sentence "enrich selectively phage displayed antibodies directed against proteins constituting a difference between two populations of cells"; *see also* Abstract, second sentence, "[a]ntibodies recognizing a defined difference between two otherwise identical protein mixtures were isolated"; *see also* Fig. 1, bottom, "phage bound to the target proteins on the immunobead(s) were rescued"; *see also* Section 3 *Results and discussion*, p. 73, right column, first paragraph, second sentence, "[t]he goal is to establish a competitive panning procedure, which can be used to obtain phage antibodies against antigens expressed differentially in different cell populations"; *see also* Section 3 *Results and discussion*, p. 73, right column, third paragraph, first sentence, "we were able to

enrich preferentially for phage that were reactive against LDH"; *see also* Section 3 *Results and discussion*, p. 74, right column, second full paragraph, first sentence, "selection against all differences");

wherein the removing step comprises contacting (see p. 71, right column, last paragraph, second sentence, "biopanning procedure") the sample (see p. 71, right column, last paragraph, second sentence, "naïve phagemid library") with an affinity binding composition (see p. 71, right column, last paragraph, second sentence, "single-chain Fv antibody fragments (scFv)") comprising:

(a) a plurality of solid phase matrices (see p. 71, right column, last paragraph, second sentence, "naïve phagemid library") (emphasis added) arranged such that each solid phase matrix is in contact with at least one other solid phase matrix (see p. 71, right column, last paragraph, second sentence, "naïve phagemid library") (emphasis added);

(b) a plurality of receptors having different protein binding specificities (see p. 71, right column, last paragraph, second sentence, "single-chain Fv antibody fragments (scFv)");

wherein the receptors (see p. 71, right column, last paragraph, second sentence, "single-chain Fv antibody fragments (scFv)") are immobilized on the plurality of solid phase matrices (see p. 71, right column, last paragraph, second sentence, "naïve phagemid library") such that each solid phase matrix has a different protein binding specificity (see p. 72, left column, Section 2.1 *Library and bacteria*, first sentence, "10^8 clones"),

wherein each solid phase matrix comprises a plurality of particles (see Section 1 *Introduction*, first sentence, "coat protein"), wherein the particles (see Section 1 *Introduction*, first sentence, "coat protein") are present in a mixture (see Fig. 1, "two solid phase system");

Claims 32, 52, 62-69, 84, 88-89, 104 and 110-113 are rejected under 35 U.S.C. 102(e) as being anticipated by Payan (US 6,455,263).

Payan describes a method for separating proteins (see col. 13, lines 1-2, "beads are then sorted using fluorescent-activated cell sorting") from a sample that contains proteins (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules") and recovering a modified sample (see col. 2, lines 64-65, "collected") comprising the steps:

(1) removing at least two specific predefined proteins (see *e.g.*, col. 13, lines 10-11, "non-fluorescent beads") from a sample that contains the at least two specific predefined proteins (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules"), thereby producing a modified sample containing a plurality of proteins (see col. 13, lines 10-11, "sorting results in a population of non-fluorescent beads and at least one population of fluorescent beads");

(2) recovering the modified sample (see col. 2, lines 64-65, "collected");

wherein the removing step comprises contacting the sample with an affinity binding composition (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules") comprising:

(a) a first and second solid phase matrix contacting each other, wherein each solid phase matrix comprises a plurality of particles (see col. 7, line 52, "bead composition"), and wherein the particles are present as a mixture (see col. 12, line 55, "reaction mixture").

With respect to claims 88 and 104, Payan describes antibody candidate agents (see col. 9, lines 39-42).

With respect to claim 89, Payan describes libraries of synthetic compounds and their generation (see col. 3, lines 51-65).

Claim Rejections - 35 USC § 103

Claims 32, 52, 62-69, 84-85, 88-89, 104-107 and 110-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davies (US 6,696,304) in view of Payan (US 6,455,263).

Davies describes a method for separating proteins (see col. 16, line 67, "screening of combinatorial libraries") comprising the step of:

(1) contacting a sample with an affinity binding composition (see col. 9, lines 48-50, "[a] test analyte/microparticle complex is added directly to the mixture of microparticles with immobilized protein standards") comprising:

(a) a plurality of solid phase matrices (see Title, "particulate solid phase") arranged such that each solid phase matrix is in contact with at least one other solid phase matrix (see col. 9, lines 48-50, "[a] test analyte/microparticle complex is added directly to the mixture of microparticles with immobilized protein standards"), and wherein each solid phase matrix (see col. 9, line 48, "[a] test analyte/microparticle complex"; col. 9, lines 49-50, "mixture of microparticles with immobilized protein standards") comprises a plurality of particles, and wherein the pluralities of particles are present as a mixture (see col. 9, lines 48-49, "added directly to the mixture"); and

(b) a plurality of receptors immobilized on the plurality of solid phase matrices (see *e.g.*, col. 14, line 52, "antibody").

Davies does not describe the steps of "removing at least two specific predefined proteins from a sample", "producing a modified sample" and "recovering the modified sample".

However, Payan describes a method for separating proteins (see col. 13, lines 1-2, "beads are then sorted using fluorescent-activated cell sorting") and recovering a modified sample (see col. 2, lines 64-65, "collected") comprising the steps:

> (2) removing at least two specific predefined proteins (see *e.g.*, col. 13, lines 10-11, "non-fluorescent beads") from a sample that contains the at least two specific predefined proteins (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules"), thereby producing a modified sample containing a plurality of proteins (see col. 13, lines 10-11, "sorting results in a population of non-fluorescent beads and at least one population of fluorescent beads"); and
>
> (3) recovering the modified sample (see col. 2, lines 64-65, "collected").

It would have been obvious for a person of ordinary skill in the art to perform the method for screening combinatorial libraries of Davies with the added procedural steps of producing and recovering a modified sample because Payan discovered that producing and recovering a modified sample using FACS allows for subsequent analysis (see col. 2, line 65), treatment (see col. 3, line 8) and/or characterization (see col. 3, line 10) of separated proteins.

With respect to claim 85, Davies describes an affinity purification column containing the affinity binding composition (see col. 17, lines 47-48, "affinity purification columns").

With respect to claims 104-107, Davies describes an affinity binding composition that binds to albumin (see col. 15, line 9), immunoglobulins (see col. 15, lines 16-19), transferrin (see col. 15, line 16), haptoglobin (see col. 15, line 15), alpha-1-antitrypsin (see col. 15, line 12), alpha-2-macroglobulin (see col. 15, line 12), alpha-1-acid glycoprotein (see col. 15, line 9), hemopexin (see col. 15, line 15),

transthyretin (see col. 15, line 14), apolipoprotein A1 (see col. 15, line 13) and prealbumin (see col. 15, line 14).

Response to Arguments

Specification

In prior Office Action, Examiner objected to the specification for failing to provide proper antecedent basis for the language "specific predefined *proteins*" as recited in claims 63 and 84.

In response, Applicants observe that the phrase "specific predefined *ligand*" is supported in originally-presented claim 27. Applicants posit that persons skilled in the art recognize that "protein" is a subset of "ligand"[5] and would immediately recognize the metes and bounds of the phrase.

Applicants' argument has been carefully considered but is not persuasive.

Although the phrase "specific predefined *ligand*" is supported in originally-presented claim 27, the phrases "specific predefined *proteins*" or "predefined proteins" are not supported in originally-presented claim 27. Originally-presented claim 27 does not identify any objects and/or steps required for "predefining" proteins, or whether predefining "proteins" is any different than predefining "ligands". Examiner posits that persons skilled in the art recognize that the objects and/or steps required for "predefining" proteins is not necessarily or inherently the same as the objects and/or steps required for predefining "proteins".

Claim Rejections - 35 USC § 112

In prior Office Action, claim 63 was rejected under 35 U.S.C. 112, second paragraph, because the phrase "solid phase matrices" lacked antecedent basis and was considered indefinite. Specifically, whether "solid phase matrices" referenced "a first and second solid phase matrix" was not clear. Applicants'

[5] Examiner requests Applicants to cite specific support in Applicants' specification, as originally filed, for Applicants' alleged set-subset relationship between "protein" and "ligand".

amendment and argumentation are fully persuasive and sufficient to overcome this rejection. Accordingly, this rejection is withdrawn.

In prior Office Action, claims 63 and 84 were rejected under 35 U.S.C. 112, second paragraph, because the phrase "each solid phase matrix comprises a plurality of particles" was considered unclear. Specifically, whether/how a bead comprises "a plurality of particles" is not clear.

In addition, claims 63 and 84 were rejected under 35 U.S.C. 112, second paragraph, because the phrases "a first and second solid phase matrix contacting each other" (claim 63) and "each solid phase matrix is in contact with at least one other solid phase matrix" (claim 84) were considered unclear. Specifically, whether/how a matrix of beads is in contact with another matrix of beads is not clear. Whether the claim limitation "contacting" or "in contact" requires a matrix of beads to be stacked, layered and/or adjoined on/to another matrix of beads is not clear. How a matrix of beads that is stacked, layered and/or adjoined on/to another matrix of beads can be "present as a mixture" is not clear.

In response, Applicants argue "[o]ne of ordinary skill in the art would understand that a single bead can constitute a complete matrix" (see Applicants' reply, p. 9, first paragraph, fourth sentence). In addition, Applicants submit that "the objected phrase, on its face alone comprises possibility of being 'in contact' includes by stacked, layered, and/or adjoined possibilities" (see Applicants' reply, p. 9, last paragraph, fourth sentence).

Applicants' arguments have been carefully considered but are not persuasive.

Applicants' reply does not appear to address whether/how a bead comprises "a plurality of particles", or whether/how a matrix of beads is in contact with another matrix of beads, or how a matrix of beads that is

stacked, layered and/or adjoined on/to another matrix of beads can be "present as a mixture". Examiner has offered suggestions for resolving these issues.[6]

Claim Rejections - 35 USC § 102

In prior Office Action, claims 32, 52, 62-69, 84, 89 and 104 were rejected under 35 U.S.C. 102(b) as being anticipated by Stausbøl-Grøn *et al.,* 391 FEBS LETTERS 71 (1996).

In response, Applicants argue:

1. Stausbøl-Grøn *et al.* teach removal of "phage", whereas the instant invention requires removal of "proteins" (see Applicants' reply, p. 10, second full paragraph, third full paragraph).
2. Even if Stausbøl-Grøn *et al.* teach removal of "proteins", Stausbøl-Grøn *et al.* do not teach removal of "at least two" proteins (see Applicants' reply, paragraph bridging pp. 10-11).
3. Stausbøl-Grøn *et al.* do not teach "recovery of a modified sample" (see Applicants' reply, p. 11, first full paragraph).
4. Stausbøl-Grøn's *et al.* description of "immunobeads" does not amount to a "first and second solid phase matrix" (see Applicants' reply, p. 11, second full paragraph).
5. Examiner has potentially extrapolated claimed limitations from the teachings of Stausbøl-Grøn's *et al.* (see Applicants' reply, paragraph bridging pp. 11-12).

Applicants' arguments have been carefully considered but are not persuasive.

With respect to argument 1), Stausbøl-Grøn *et al.* teach the removal (see Section 3 *Results and discussion*, p. 74, right column, second full paragraph, first sentence, "selection inhibition of all similarities") of proteins (see p. 71, right column, last paragraph, second sentence, "single-chain Fv antibody fragments (scFv)"; *see also* Section 1 *Introduction*, first sentence, "coat protein"). That Stausbøl-Grøn *et al.* incidentally teach proteins that are attached to a phage does not negate Stausbøl-Grøn's *et al.* description of protein removal.

[6] See *supra*, notes 1-4.

With respect to argument 2), Stausbøl-Grøn *et al.* teach the removal of at least two proteins (see Section 3 *Results and discussion*, p. 74, right column, second full paragraph, first sentence, "selection inhibition of all similarities"; *see also* last sentence, "as many proteins as possible") (emphasizing plurality of proteins) from a sample.

With respect to argument 3), Stausbøl-Grøn *et al.* teach producing and/or recovering a modified sample (see Abstract, first sentence "enrich selectively phage displayed antibodies directed against proteins constituting a difference between two populations of cells"; *see also* Abstract, second sentence, "[a]ntibodies recognizing a defined difference between two otherwise identical protein mixtures were isolated"; *see also* Fig. 1, bottom, "phage bound to the target proteins on the immunobead(s) were rescued"; *see also* Section 3 *Results and discussion*, p. 73, right column, first paragraph, second sentence, "[t]he goal is to establish a competitive panning procedure, which can be used to obtain phage antibodies against antigens expressed differentially in different cell populations"; *see also* Section 3 *Results and discussion*, p. 73, right column, third paragraph, first sentence, "we were able to enrich preferentially for phage that were reactive against LDH"; *see also* Section 3 *Results and discussion*, p. 74, right column, second full paragraph, first sentence, "selection against all differences");

With respect to argument 4), Stausbøl-Grøn *et al.* provide three different interpretations of a "first and second solid phase matrix". For example:

> (a) Stausbøl-Grøn *et al.* teach a first and second solid phase matrix (see Fig. 1, "two solid phase system") contacting each other (see Fig. 1, "immunobeads in an immunotube"), wherein each solid phase matrix comprises a plurality of particles (see Fig. 1, "immunobeads in an immunotube"), wherein the particles are present in a mixture (see p. 72, col. 1, sixth paragraph, "4 ml 2% MPBS... five immunobeads... were added");

(b) Stausbøl-Grøn *et al.* teach a plurality of solid phase matrices (see p. 71, right column, last paragraph, second sentence, "naïve phagemid library") (emphasis added) arranged such that each solid phase matrix is in contact with at least one other solid phase matrix (see p. 71, right column, last paragraph, second sentence, "naïve phagemid library") (emphasis added);

(c) Stausbøl-Grøn *et al.* teach a "first and second solid phase matrix", wherein "solid phase matrix" = a bead (see specification p. 9, lines 10-11, "[a] suitable matrix is, for example a bead or a microbead shape") (emphases added).

With respect to argument 5), Examiner has clarified his grounds for rejection to avoid the appearance of potentially extrapolating claim limitations from the teachings of Stausbøl-Grøn's *et al.* See *supra*, rejection of claims 32, 52, 62, 84, 89 and 104 under 35 U.S.C. 102(b) in view of Stausbøl-Grøn *et al.*, 391 FEBS LETTERS 71 (1996). Examiner's clarified grounds for rejection avoids relying upon the specific set of experiments performed by Stausbøl-Grøn *et al.* and the specific data obtained therefor. Examiner's clarified grounds for rejection attempts to give deference to the broader analytical framework affirmatively established (*i.e.*, not "extrapolated") by Stausbøl-Grøn *et al.*, namely, the analysis of differential gene expression (see Title, "A model phage display substraction method with potential for analysis of differential gene expression") (emphasis added).

According to MPEP 2123, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments.

Examiner posits that persons of ordinary skill, upon a thorough reading and understanding of the teachings of Stausbøl-Grøn *et al.*, would conclude that the broader analytical framework affirmatively established (*i.e.*, not "extrapolated") by Stausbøl-Grøn *et al.* was not to isolate a single phage antibody against LDH, but rather to establish a model system (see Title, "A model phage display subtraction method"; see p. 71, col. 2, last paragraph, "[a] competitive biopanning procedure was developed and

tested on two model systems") to be used for isolating multiple phage antibodies against differentially expressed proteins (see p. 71, col. 2, last paragraph, "the subtractive strategy presented is valuable in attempts to identify antibodies against known or unknown antigens in a given population of cells", noting Brian's *et al.* use of plural "antibodies" and "antigens").

In prior Office Action, claims 32, 52, 62-69, 84, 88-89 and 104 were rejected under 35 U.S.C. 102(e) as being anticipated by Payan (US 6,455,263).

In response, Applicants argue that Payan does not teach:

1. removal of two specific proteins;
2. recovery of a modified sample; and
3. a first and a second solid phase matrix comprising a first receptor and a second receptor.

Applicants' arguments have been carefully considered but are not persuasive.

With respect to argument 1), Payan describes a method for separating (see col. 13, lines 1-2, "beads are then sorted using fluorescent-activated cell sorting") proteins (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; *see also* col. 14, lines 24-25, "third, fourth, etc. populations of target molecules"; *see also* col. 3, lines 28-30, "[b]y 'candidate bioactive agent' or 'candidate drugs' or grammatical equivalents herein is meant any molecule, e.g. protein").

With respect to argument 2), Payan describes recovering a modified sample (see col. 2, lines 64-65, "collected"; *see also* col. 13, lines 10-11, "sorting results in a population of non-fluorescent beads and at least one population of fluorescent beads").

With respect to argument 3), Payan describes an affinity binding composition (see *e.g.*, col. 3, lines 48-49, "library of candidate agents"; col. 14, lines 24-25, "third, fourth, etc. populations of target molecules") comprising a first and second solid phase matrix contacting each other (see col. 7, line 52, "bead composition"), wherein each solid phase matrix comprises a plurality of particles (see col. 7, line 52, "bead composition"), and wherein the particles are present as a mixture (see col. 12, line 55, "reaction mixture"). Each of the solid phase matrices comprises a receptor (see col. 3, lines 48-49, "library of candidate agents").

Claim Rejections - 35 USC § 103

In prior Office Action, claims 32, 52, 62-69, 84-85, 88-89 and 104-107 were rejected under 35 U.S.C. 103(a) as being unpatentable over Davies (US 6,696,304) in view of Payan (US 6,455,263).

In response, Applicants argue that Davies does not teach:

1. Davies does not teach preparation of a mixture of particles comprising different receptors;
2. Davies does not teach a mixture of solid phase matrices comprising a plurality of particles;
3. Payan does not teach removal of two specific proteins;
4. Payan does not teach recovery of a modified sample; and
5. Payan does not teach a first and a second solid phase matrix comprising a first receptor and a second receptor.

Applicants' arguments have been carefully considered but are not persuasive.

With respect to arguments 1), 2) and 5), Davies describes a plurality of solid phase matrices (see Title, "particulate solid phase") in a mixture (see col. 9, lines 48-50, "[a] test analyte/microparticle complex is added directly to the mixture of microparticles with immobilized protein standards" (emphasis added); *see*

also col. 9, lines 48-49, "added directly to the mixture"). The plurality of solid phase matrices have immobilized receptors (see *e.g.*, col. 14, line 52, "antibody").

With respect to arguments 3) and 4), Payan describes removing (see col. 13, lines 10-11, "sorting results in a population of non-fluorescent beads and at least one population of fluorescent beads") proteins and recovering (see col. 2, lines 64-65, "collected") a modified sample.

It would have been obvious for a person of ordinary skill in the art to perform the method for screening combinatorial libraries of Davies with the added procedural steps of producing and recovering a modified sample because Payan discovered that producing and recovering a modified sample using FACS allows for subsequent analysis (see col. 2, line 65), treatment (see col. 3, line 8) and/or characterization (see col. 3, line 10) of separated proteins.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv

LONG V. LE 09/01/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600